The Percentiler and Flagger Programs

Modern quality assurance tools –

web-based monitoring of performance and test stability in relation to the flagging rate as surrogate medical decision
Introduction

The Percentiler/Flagger applications in view of the already existing quality assurance efforts

Short reflections on:
• Internal quality control (IQC)
• External quality assessment (EQA)
IQC is the laboratory’s quality assurance backbone; nevertheless, IQC has limitations when commercial samples are used:

- Laboratory performance is only assessed at the peer group level
- Information about assay trueness may be jeopardized by non-commutability issues
- Reagent lot changes may affect control- and patient samples differently
- IQC samples may not be available at medically relevant concentrations
Introduction

“Ideal” EQA with commutable materials gives information of assay trueness; nevertheless, it also has limitations:

• Materials and logistics are expensive

• Typically EQA is conducted at low frequency which misses effects such as lot-to-lot changes or calibration

• Information for the laboratory is delayed

• “Traditional” EQA with non-commutable samples has the same limitations as IQC
The Percentiler/Flagger programs

Respond to these limitations:

- “Sampleless” web-based programs using data from analyses of patient samples
- “One-time” effort to join
- User interfaces allow dynamic on-line monitoring of mid- to long-term stability of performance and flagging rate
- Demonstrate the influence of factors like lot-to-lot changes or calibration
- Add value to IQC by confirming that observations also apply for patient samples, or revealing missed features
- Peer group comparisons are possible
- Combination of the two programs relates the quality of analytical performance to the effect on medical decision

The Percentiler/Flagger strengthen the laboratory, manufacturer and clinician interfaces
The Percentiler/Flagger programs

Concept/Design:

- **MySQL database**: built from daily medians of patient results (Percentiler) and % of results flagged against locally used decision points (Flagger)

- **User interface**: shows the moving medians over time for on-line monitoring of the mid- to long-term stability of performance (Percentiler) and the effect of analytical variation on the flagging rate (Flagger)

Analytes covered:

Twenty clinical chemistry analytes
Two thyroid hormones
Recent expansion with 16 analytes: basic hematology, HbA1c, IgG/M/A, ferritin, vitamin B12, folic acid, etc.
Requirements for the laboratory

Data stratification:

- Instrument or module-specific
- Outpatients

*NOTE: Stratification possible with modern Laboratory Information Systems (LIS)*
Requirements for the laboratory

Calculations:

• Instrument- or module-specific daily medians
• Percentage of flagged results (hypo and hyper)

Data transmission:

Electronic transmission of the data to dedicated e-mail addresses
(preferably daily, but less frequent reporting is possible)

Currently three formats of reporting possible:
• Embedded in the e-mail
• Attached text file
• Attached Excel® file
### Example of data transmission, Excel attachment to an e-mail

<table>
<thead>
<tr>
<th>Lab ID</th>
<th>Date</th>
<th>Instrument ID</th>
<th>Outpatient code</th>
<th>Analyte</th>
<th>Unit</th>
<th>Patient median</th>
<th>Number of results measured</th>
<th>%-hypo</th>
<th>%-hyper</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>COBAS1</td>
<td>PHT</td>
<td>TP</td>
<td>g/L</td>
<td>70.50</td>
<td>6</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>COBAS1</td>
<td>PHT</td>
<td>TSH</td>
<td>mIE/L</td>
<td>1.60</td>
<td>89</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>COBAS1</td>
<td>PHT</td>
<td>URAT</td>
<td>µmol/L</td>
<td>301.00</td>
<td>29</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>ALAT</td>
<td>U/L</td>
<td>21.00</td>
<td>134</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>ALB</td>
<td>g/L</td>
<td>46.00</td>
<td>31</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>ALP</td>
<td>U/L</td>
<td>71.00</td>
<td>89</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>ASAT</td>
<td>U/L</td>
<td>22.00</td>
<td>36</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>CA</td>
<td>mmol/L</td>
<td>2.42</td>
<td>47</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>CL</td>
<td>mmol/L</td>
<td>104.00</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AVDKOD</td>
<td>01.01.2017</td>
<td>ARCHI1</td>
<td>PHT</td>
<td>CRP</td>
<td>mg/L</td>
<td>1.90</td>
<td>63</td>
<td>0</td>
<td>19</td>
</tr>
</tbody>
</table>
And another example of data transmission

<table>
<thead>
<tr>
<th>Patient median</th>
<th>Unit</th>
<th>Analyte</th>
<th>Outpatient code</th>
<th>Instrument ID</th>
<th>Date</th>
<th>Lab ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCDEF</td>
<td>08/04/2015</td>
<td>COBAS8000C1</td>
<td>POL</td>
<td>ALB</td>
<td>g/L</td>
<td>ABCDEF</td>
</tr>
<tr>
<td>ABCDEF</td>
<td>08/04/2015</td>
<td>COBAS8000C1</td>
<td>POL</td>
<td>ALB</td>
<td>g/L</td>
<td>ABCDEF</td>
</tr>
<tr>
<td>ABCDEF</td>
<td>08/04/2015</td>
<td>COBAS8000C2</td>
<td>POL</td>
<td>ALT</td>
<td>U/L</td>
<td>ABCDEF</td>
</tr>
<tr>
<td>ABCDEF</td>
<td>08/04/2015</td>
<td>COBAS8000C1</td>
<td>POL</td>
<td>CA</td>
<td>mmol/L</td>
<td>ABCDEF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>%-hypo</th>
<th>%-healthy</th>
<th>%-hyper</th>
<th>Number of results measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>86%</td>
<td>14%</td>
<td>35</td>
</tr>
<tr>
<td>0%</td>
<td>87%</td>
<td>15%</td>
<td>37</td>
</tr>
<tr>
<td>0%</td>
<td>90%</td>
<td>10%</td>
<td>126</td>
</tr>
<tr>
<td>0%</td>
<td>72%</td>
<td>28%</td>
<td>57</td>
</tr>
<tr>
<td>4%</td>
<td>96%</td>
<td>0%</td>
<td>119</td>
</tr>
<tr>
<td>6%</td>
<td>94%</td>
<td>0%</td>
<td>102</td>
</tr>
</tbody>
</table>
Laboratory IT requirements

Automatic and hassle free calculation and electronic transmission via middleware, Laboratory Information System (LIS) or laboratory self-made solution

- LIS solutions already available: from GLIMS (MIPS), CorLabs (Cegeka), MOLIS (Vision4Health Belgium S.A.), FONS Openlims (STAPRO Ltd.), Modulab (Systelab Technologies, S.A.), Swisslab* (Roche Diagnostics)

- *R-script to extract/send laboratory data from Swisslab at https://github.com/acnb/SwlToEmpower (by courtesy: A. Bietenbeck, MD, PhD, TU München)
Tools provided by the organizers

Software and MySQL database
• Mapping of laboratory-specific codes (for laboratory ID, instruments, analytes)/units
• Automatic reading of e-mails and transfer to the database
• Grouping of laboratories in peer groups

Graphical user interfaces
• Accessible with laboratory-specific login/password
• Show instrument- or module-specific moving medians in time (of the individual laboratory; peer group)
• Show zones for stable performance/flagging based on quality goals

Peer group overviews
Quality goals

Percentiler:
- If possible, based on biological variation
  - e.g. for total cholesterol, allowable bias 4% (0.2 mmol/L at a median of 4.90 mmol/L)
- If not feasible (e.g., for analytes with tight biological control), bias goal based on state-of-the-art performance
  - e.g. for sodium, 0.7% (1 mmol/L at a median of 140.6 mmol/L)

Flagger:
Analyte-specific limits expressed relatively to the long-term flagging rate, but with an absolute minimum of 1%; e.g., for AST the limit is set at 30%:
  - If the flagging rate is 10%, limit = ± 3% (30% of 10%)
  - If the flagging rate is 2.5%, limit = ± 1% (NOT 0.75%)
User interface – Percentiler

https://www.thepercentiler.be

Login: User = DEMOLAB, password = demo1234
User interface – Percentiler

Legend:
- Moving median from Jan 2014 til Jan ’16 for two instruments in a laboratory.
- Grey dotted line: the laboratory’s long-term median.
- Black dotted line: the peer group moving median.

NOTE: plots can be downloaded by users.
Percentiler – selected examples

Identifies stable performance for calcium in the selected laboratory and peer group (see the moving medians within the limits of the stability zone)
Percentiler – selected examples

Identifies unstable performance for ALT–GPT in the selected laboratory and peer group due to the effect of lot-to-lot changes (see the shifts of the moving medians outside the limits of the stability zone)
Percentiler – selected examples

Identifies unstable performance for total-protein in the selected laboratory due to reagent instability requiring recalibration (see the typical saw tooth pattern of the moving median)
Percentiler – selected examples

Identifies unstable performance for chloride in the selected laboratory (peer group not affected) due to electrode deterioration and recalibration (problem solved after electrode replacement)
Percentiler – selected examples

Identifies that the selected laboratory is biased relative to the peer group for sodium
Percentiler – selected examples

Demonstrates poor preanalytics for potassium (the effect of the temperature on the medians: high in winter, low in summer, opposite to the temperature)
User interface – Flagger

https://www.thepercenntiler.be

Login: User = DEMOLAB, password = demo1234
User interface – Flagger

Legend:
- Moving median of % hypo and hyper flagging rate from July 2014 to Nov ‘14 for two instruments in a laboratory.
- Grey dotted line: the median of the laboratory’s long-term flagging rate.

The shaded zone reflects stable flagging rate; for the calcium example the limits of the zone are at ± 70% of the median for the long-term flagging rate.
Percentiler & Flagger synergy

Demonstrates the effect of analytical instability on the flagging rate as surrogate of medical decision

Explanation:
- Left hand plot in the Percentiler; the yellow instrument has stable performance for calcium; in contrast, the red one shows a shift of ~0.06 mmol/L.
- Right hand plot in the Flagger: the hyper flagging rate for the yellow instrument is stable, while for the red one it is triplicated (median from 2.5% to 7.5%).
The way forward

Hosting of the programs by NOKLUS:

• Further development by IT programmers
• Confidentiality ensured (agreement can be made)
• Establishment of an international advisory group
• Meetings with users to better address their needs
• Discussion of the role of the programs for IQC/EQA with specialists in laboratory medicine, national EQA organisers and through the EQALM platform
• Linda Thienpont/Dietmar Stöckl (Thienpont & Stöckl Wissenschaftliches Consulting GbR) will be our consultants on the programs and aid with further development
Interested?

Contact us:

Anne Elisabeth Solsvik
Anne.elisabeth.solsvik@noklus.no
📞 +47 97 95 00


